

Proceeding Paper

# Public Health Implications of Antimicrobial Resistance in Wildlife at the One Health Interface <sup>†</sup>

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**Abstract:** Antimicrobial resistance (AMR) such as extended-spectrum beta-lactamase (ESBL)-producing and carbapenem-resistant (CARBA) *Enterobacterales* is a main global cause of human deaths and a major health burden to domestic animals. AMR circulation in wildlife has also been reported worldwide, but the public health impact and the policy actions that could limit this circulation remain unknown. Here, we summarize the key trends of AMR in wildlife, clarify the use of the term ‘reservoir’ when referring to AMR in wildlife, identify whether national plans to tackle AMR in Latin America and Europe include wildlife, and discuss the public health implications of this circulation. We provide recommendations for AMR surveillance and prevention among wild animals, as well as the key scientific knowledge gaps that are hindering understanding its dynamics. We expect our conclusions to shed light on the necessity and degree of prevention and control regarding AMR in wildlife at the human–animal–environment interface.

**Keywords:** antimicrobial resistance; wild animals; surveillance; policy makers; national plans



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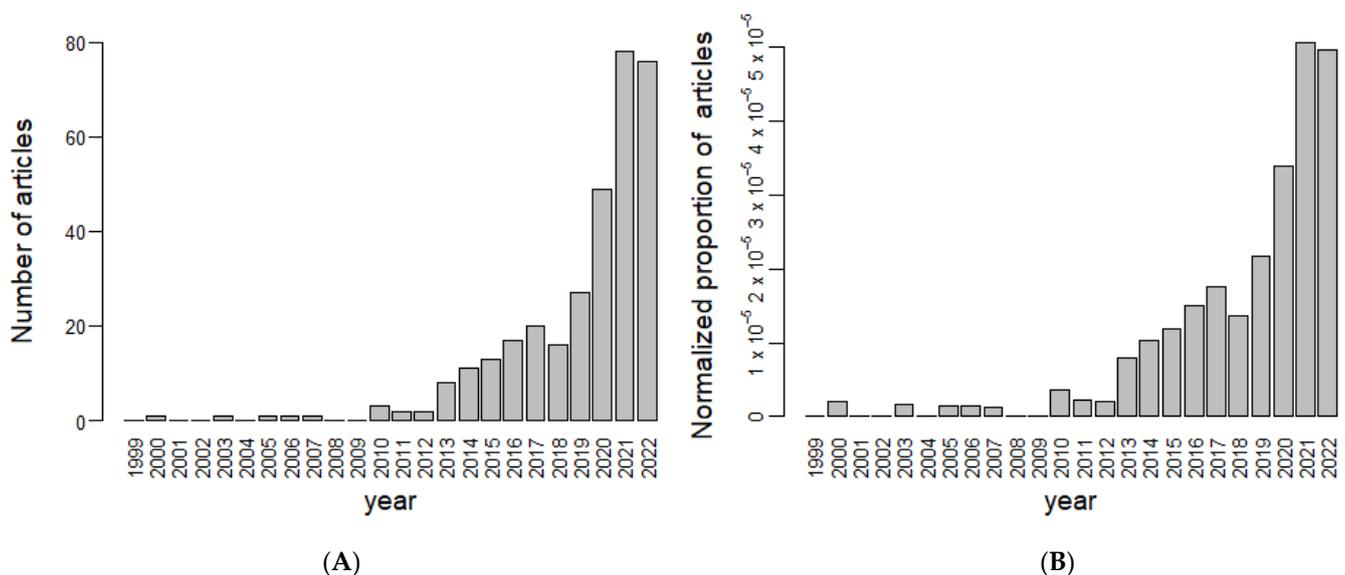
## 1. Introduction

Antimicrobial resistance (AMR) is a global One Health challenge affecting the health of humans and domestic animals and is spreading to natural environments, including wildlife [1–3]. For example, extended-spectrum beta-lactamases (ESBLs) and carbapenemase (CARBA)-producing *Enterobacterales*, pathogens of critical importance for public health, have been reported in wildlife living closely to humans such as gulls, storks, bats, and rodents [4–8]. Therefore, wildlife are often referred to as ‘reservoirs’, ‘disseminators’, ‘vectors’, or ‘sentinels’ of AMR, without a clear understanding of the implications of these terms for public health [7,9–11]. AMR surveillance in wildlife remains limited, and there is no systematic information on which national and international plans to combat AMR have implemented AMR surveillance among wild animals.

Given the rising reports of AMR in wildlife [3] and the One Health approach promoted to combat AMR, including the environmental component [12], this perspective aims to summarize key trends in the reports of AMR in wildlife, identify if national and regional plans to combat AMR in Latin America and Europe include surveillance in wild animals, and discuss the public health implications of this circulation. We also advise policy makers to evaluate if the surveillance and control of AMR in wildlife in their local context is necessary, realistic, and cost-effective.

## 2. Rising Reports of AMR in Wildlife

AMR reports in wildlife, particularly fecal carriage of *Enterobacterales*, have been published globally in different animal groups including birds, mammals, and reptiles [7,9,13]. For example, a review on the role of gulls in AMR conducted in 2021 showed that three out of four antibiotic-resistant pathogens considered as a “critical priority” by the WHO have been identified in gulls [13]. Similarly, MRSA has been detected in several wild species [14]. The number of scientific articles on antimicrobial resistance and wildlife keeps increasing, particularly since 2012 (Figure 1) [3]. Despite hundreds of studies on wildlife and the overall assumption that this AMR comes from ‘environmental pollution’ of humans or domestic animals, the pathways of transmission at the One Health interface have been poorly identified, and very few studies have actually tested if wild animals can maintain and spread AMR across landscapes and geographical regions or contaminate humans and domestic animals [10,13]. This question of potential ‘spillback’ from wildlife to humans or domestic animals remains a key aspect in evaluating the implications of their AMR carriage for public and animal health. Moreover, the health consequences of AMR colonization in wildlife (e.g., microbiome changes) or ‘clinical resistance’ (e.g., treatment failure in rehabilitation centers) remain poorly understood [15]. In fact, very few studies have evaluated how wild animals respond to treatment with antibiotics. For example, changes in the microbiome were evaluated after treatment of wild western lowland gorillas (*Gorilla gorilla gorilla*) with ceftiofur following a respiratory disease outbreak [16]. However, to our knowledge, there are no studies on the percentage of treatment failures associated with AMR in rescue and rehabilitation wildlife centers. Thus, the consequences of AMR for wildlife conservation remain unknown. Likewise, the potential for new AMR and virulent bacteria to ‘mix’ in wildlife and generate new strains of public health concern (e.g., *Salmonella* in wild birds acquiring multidrug resistance and spreading during contact with domestic birds) has been proposed as a potential threat to public health [9,10], but remains unstudied. Thus, filling these knowledge gaps and clarifying the role of wildlife in AMR spread are essential to properly evaluate the public health implications and policy decisions to be taken given the recent findings of AMR among wild animals.



**Figure 1.** Number of studies including ‘antimicrobial resistance’ and ‘wildlife’ in their title and abstract published in PubMed between 1999 and 2022. (A) The number of articles per year was counted using the RISmed package in R and the query ‘Antimicrobial resistance [Title/Abstract] AND wildlife [Title/Abstract]’. The year 2023 was excluded given incomplete information. (B) The number of articles obtained in (A) was normalized (divided) by the total number of articles published in PubMed per year.

### 3. Are Wild Species Really a 'Reservoir' of AMR and/or 'Sentinels' of Environmental Pollution?

There are several definitions and misinterpretations of the term 'pathogen reservoir' in the public health, veterinary, and disease ecology literature [17,18]. For bacteria such as *E. coli*, the term reservoir can also be used at different scales; e.g., the human gut and domestic animals have been defined as reservoirs of extraintestinal pathogenic *E. coli* in humans [19,20]. Haydon et al. (2002) defined a reservoir "as one or more epidemiologically connected populations [...] in which the pathogen can be permanently maintained and from which infection is transmitted to the defined target population" [18]. In the context of AMR, we could adapt this definition of a reservoir to 'one or several wild populations capable of maintaining AMR and transmitting it to humans or domestic animals' considered as target populations. For some pathogens such as viruses, the simple detection of a viral disease in a new host can be rapidly assessed as a consequence of spillover from a wild (but perhaps unknown) reservoir (e.g., Ebola and SARS-CoV spillover to humans by bats or an intermediate wild host [21], or avian influenza spillover from wild birds to domestic birds or humans [22]). However, since several bacteria like *E. coli* are already present in most animals, the simple presence of these bacteria or its AMR mechanism (e.g., CARBA- or ESBL-resistant genes) is not sufficient proof of cross-species transmission or a spillover event [9,23]. In fact, these bacteria can be circulating independently among different host groups living in proximity (e.g., antibiotic-resistant *Salmonella* mostly circulates independently in both humans and livestock in Scotland [24]). Therefore, additional information such as genomic sequencing of detected antibiotic-resistant strains to estimate genetic differences (e.g., number of SNP difference), AMR gene identities, and other traits (e.g., virulence genes and plasmids) is needed to suggest potential cross-species transmission, for example, between wild animals and humans. Moreover, the direction of this transmission is complex to determine and mostly assumed (e.g., from humans to wild animals) with little scientific proof of their origin, pathway, or frequency [13]. The lack of a clear definition and scientific evidence for the use of 'reservoir' referring to AMR in wildlife precludes a solid understanding of the need to prevent AMR circulation and spillover to humans and of the public health benefits of such preventive measures. For example, limiting farm-to-farm transmission of CARBA-resistant *E. coli* by wild birds could be of minimal impact to public health if the prevalence of circulation of CARBA-*E. coli* is already high between these farms. However, long distance transmission of these same bacteria by gulls could have important public health impacts if transmission happens from an area with a high prevalence of CARBA-*E. coli* to an area with a low prevalence and if these bacteria establish in the new area and promote clinical treatment failure. Therefore, AMR spread by wildlife could become an issue mainly in target populations where AMR is inexistent or has been reduced to low levels relative to the potential spillover of AMR from wildlife. In fact, this is likely already generated by human transport across the globe [25]. A more environmental perspective on AMR considers it as 'environmental pollution' [26,27] and addresses the need for AMR surveillance in 'sentinel' wildlife as a method to monitor the impact of human activities on natural environments. This is also a relevant topic but requires a study of the impacts (at the individual and population level) of this contamination in wild populations, which, to our knowledge, has not been conducted.

### 4. Surveillance of Wildlife in National Action Plans (NAPs) of AMR

To enhance the AMR response, the Quadripartite (FAO, WHO, OIE, and UNEP) promotes One Health within national action plans (NAPs), incorporating wildlife in cross-sectoral initiatives [28]. We assessed the "Global Database for Tracking AMR Country Self-Assessment Survey" to identify NAPs, including wildlife in Europe and Latin America [29]. We collected data on the establishment of integrated surveillance involving environment and animal sectors. Detailed information was obtained from officially approved NAP documents available online in the WHO Library [30], including the presence

of the keywords: “One Health”, “environment”, “wildlife”, “wild animal”, “biodiversity”, and “natural fauna” (Table 1). We manually looked for the most recent NAP when the information in the WHO library seemed out of date (e.g., the WHO library does not include the latest NAP in Spain).

**Table 1.** List of countries with a national action plan (NAP) on AMR and their inclusion or not of the One Health and wildlife components.

Region (Number of Countries with a NAP)	Wildlife Mentioned in the NAP	Integrated Surveillance with the Involvement of the Environmental and/or Animal Sectors	Wildlife Surveillance in the NAP (Execution)
Europe (n = 44)	Austria, Ireland, Italy, Norway, Spain, and Switzerland	Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Kazakhstan, Kyrgyzstan, Luxembourg, Malta, Netherlands, Norway, Portugal, Romania, Russian Federation, Slovakia, Spain, Sweden, Tajikistan, United Kingdom, and Ukraine	Austria (yes, surveillance on hunted animals for human consumption), Ireland (yes, research on AMR in native wildlife), Norway (no), Spain (no).
Latin America (n = 22)	Costa Rica	Argentina, Chile, Cuba, El Salvador, Jamaica, Mexico, Paraguay, and Peru	None

Half of the European (22 out of 44) and Latin American countries (10 out of 22) have NAPs reporting policy objectives aligned with a One Health approach. However, only seven (six in Europe and Costa Rica in Latin America) mentioned wildlife (Table 1). Based on the publicly available NAPs, we identified two countries executing wildlife-related activities. Austria is conducting wildlife surveillance, albeit limited to hunted wild animals intended for food. Likewise, Ireland reported exploring the role of native Irish wildlife species in AMR transmission during the first year of their NAP implementation, and there are plans to expand these efforts in the coming years to generate supporting evidence for the development and implementation of effective prevention and risk management strategies. Norway intends to study AMR in wild animals and non-antibiotic factors contributing to AMR in natural environments (e.g., disinfectants). Spain has also established an “Environmental Resistance” working group to investigate AMR in the natural environment. While most of the document provides a comprehensive bibliography, the group encourages further research on exposure sources in wildlife. In the NAPs of Italy, Switzerland, and Costa Rica, mentions of wildlife were limited to the introduction sections. Despite recognizing the potential role of wild animals in AMR spread due to increasing human–animal–environment overlap, their NAPs do not seem to prioritize wildlife surveillance in the coming years. The importance of environmental surveillance was documented in 39 NAPs (29 in Europe and 10 in Latin America). However, it was not clear if “environmental surveillance” included wildlife. Therefore, while many countries have embraced the One Health concept to mitigate AMR [31], the inclusion of wildlife surveillance in NAPs is almost inexistent.

**5. Conclusions and Recommendations: Should We Survey and Prevent/Control AMR in Wildlife?**

Although the increasing reports of AMR in wildlife have several potential public health, environmental, and economic implications, there are still several scientific gaps that prevent determining if these implications are taking place. For example, it remains uncertain if wildlife are actually reservoirs of AMR and whether there are concrete implications of AMR for wildlife health. Thus, we recommend that the One Health national plans to combat AMR identify gaps to be filled in order to evaluate whether AMR surveillance in wildlife should be undertaken, the specific goals of such surveillance, and whether surveillance will be the first step in establishing future preventive measures (e.g., if wild animals

have increased contact with a given human or domestic animal population). We provide the following recommendations to be discussed by different stakeholders regarding the inclusion of wildlife in AMR national plans within a One Health approach:

- (a) Identify and prioritize bacterial pathogens, animal groups, and scenarios of wildlife–human–domestic animal interactions where the circulation of AMR in wildlife could have significant public health and economic implications.
- (b) Categorize wild species according to their degree of spatial dispersion (e.g., migratory vs. resident species) and contact intensity with other species (e.g., frequent vs. infrequent habitat sharing with humans) to predict their potential to spread AMR.
- (c) Evaluate the cost-effectiveness of AMR surveillance of wildlife compared to the absence of surveillance, evaluating different methods such as targeted surveillance in specific animal groups or reinforcing surveillance if AMR reaches a given prevalence in wildlife.
- (d) Fund and design studies aiming to understand the level of potential treatment failures associated with AMR circulation in wildlife rehabilitation/rescue centers, as well as the actual health consequences of AMR for wild animals (e.g., changes in microbiota).
- (e) Pilot wildlife AMR surveillance with a One Health approach in a well-known system with available data on humans and domestic animals.
- (f) Specify terminology and avoid the unnecessary use of the term ‘reservoir’, which could have negative implications for wildlife (e.g., negative actions from local stakeholders related to fear of disease).

Overall, AMR prevention and control in wildlife can be seen as a complex, ‘wicked’ public health and conservation problem with ‘no consensus regarding the problem definition’, ‘involving multiple stakeholders’ and ‘no clear solution’ [32]. Therefore, we promote the co-creation of transdisciplinary solutions with stakeholders from disciplines such as wildlife ecology, wildlife management, veterinary, microbiology, agriculture, social sciences, and public health.

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